Considerations in nerve repair

LARRY M. WOLFORD, DMD, AND EBER L. L. STEVAO, DDS, PhD

Some nerve injuries require repair in order to regain sensory or motor function. Although this article focuses primarily on trigeminal nerve (TN) injuries and repairs, the facts presented may apply to any peripheral nerve repair.

The primary indications for nerve repair or grafting are 1) an injury or continuity defect in a nerve, as a result of trauma, pathology, surgery, or disease, that cannot regain normal function without surgical intervention and 2) loss of normal neurologic function, resulting in anesthesia, paresthesia, dysesthesia, or paralysis, that cannot be corrected by nonsurgical treatment.

In some nerve injuries (e.g., neurapraxia), the nerve regains sensory or motor function unless irreversible compression, neuroma (axonotmesis), or transection (neurotmesis) occurs. In more severe injuries, there may be significant loss of nerve substance (continuity defect), or a section of nerve may need to be removed to expose normal nerve tissue in preparation for nerve repair. Thus, nerve repair and nerve grafting procedures may be required to provide continuity between the proximal and distal portions of the nerve.

The 3 major branches of the TN that can be involved in injuries are the inferior alveolar nerve (IAN), lingual nerve (LN), and infraorbital nerve (ION). The most common types of injury to the IAN and LN are iatrogenic, related to removal of impacted teeth (*Figure 1*), orthognathic surgery (jaw repositioning), periodontics (gum surgery), endodontics (root canal procedures), dental implants, curettage of intrabony lesions, partial

or total resection of the mandible or tongue in tumor removal, and other surgical procedures. Injuries to the ION are more commonly caused by trauma to the middle third of the face, partial or total maxillectomy and orbital exenteration during resection of benign or malignant tumors, or inadvertent nerve injury during maxillary and midface osteotomy procedures. Nerve injuries that are more difficult to manage include severe stretch injuries and chemical injuries such as those that occur when alcohol, steroid, or other caustic agents are injected into or around nerves. The nature and extent of the nerve pathology will influence the type and quality of repair (1).

CONSIDERATIONS FOR DIRECT NERVE REPAIR

When surgical repair is required for a transected nerve or a nerve injury requiring excision, the best results, when conditions permit, are achieved with a direct nerve repair, without grafting. There are basically 3 types of nerve repair.

Perineurial repair involves repairing the individual fascicles and placing sutures through the perineurium. Complications of this technique include trauma to the nerve in dissecting out each fascicle and fibrosis that develops because of the dissections and numerous sutures placed. The TN branches have nongrouped fascicles.

Group funicular repair involves repairing grouped fascicles with sutures placed through the intraneural epineurium, aligning groups of fascicles. This technique is applicable only when fascicles are grouped.

Epineurial repair involves aligning the nerve ends and placing sutures through the epineurium only. Since the TN branches are polyfascicular (multiple, different-sized fascicles) and nongrouped, the epineurial technique is the most logical choice of repair method for this nerve.

CONSIDERATIONS FOR AUTOGENOUS NERVE GRAFTS

When continuity defects are present in the injured nerve or created in preparation of the nerve for repair, a nerve graft procedure may be indicated. The 2 most common donor nerves for TN repair are the sural and the great auricular nerves. Selection of a donor nerve is predicated in part on ease of harvesting and
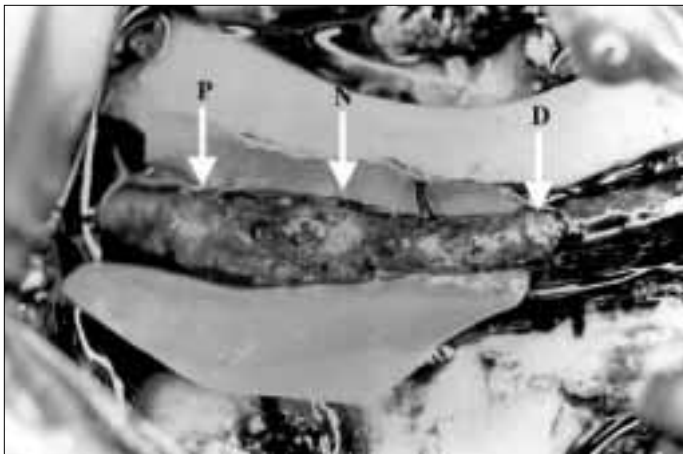
Figure 1. A large traumatic neuroma (N) is seen 1 year after removal of the third molar. Note the significant atrophy of the distal (D) portion of the nerve and the mismatch in size compared with the proximal (P) portion of the nerve.

From the Department of Oral and Maxillofacial Surgery, Baylor College of Dentistry and Baylor University Medical Center, Dallas, Texas.

Corresponding author: Larry M. Wolford, DMD, 3409 Worth Street, Suite 400, Dallas, Texas 75246 (e-mail: lwolford@swbell.net).

on minimizing postsurgical symptoms associated with the donor nerve and its functional distribution. Both the sural and great auricular nerves are relatively easy to harvest but yield localized areas of sensory deficit after surgery. Other potential donor nerves include the saphenous dorsal cutaneous branch of the ulnar, medial antebrachial cutaneous, lateral antebrachial cutaneous, superficial branch of the radial, intercostal, and other branches of the cervical plexus (2, 3). Several factors that are important to consider when selecting a donor nerve are addressed below.

Diameters of donor and host nerves. Ideally, the diameter of the nerve graft should correlate exactly with the diameter of the proximal and distal ends of the prepared host nerve. The average diameter of the IAN is 2.4 mm (4, 5); the LN, 3.2 mm (6); the sural nerve, 2.1 mm (7); and the great auricular nerve, 1.5 mm (4). For IAN grafting, the sural nerve is generally considered the best cross-sectional match because its diameter is 87% that of the IAN. However, the diameter of the sural nerve is only 66% that of the LN. The great auricular nerve diameter is about 63% and 47% of the IAN and LN diameters, respectively. The great auricular nerve works best if placed as a cable graft (*Figure 2)*, with 2 or more parallel graft strands, so the combined diameter of the 2 strands would be adequate (125% of the IAN diameter and 94% of the LN diameter).

Length of nerve graft required. It may be difficult to obtain a graft longer than 2 to 4 cm from the great auricular nerve. Since the great auricular nerve is generally half the diameter of the IAN and LN, a 2-strand cable graft usually works best for diameter match. Therefore, it may be difficult to graft a defect larger than 1 to 1.5 cm if the graft is harvested unilaterally. The sural nerve is larger in diameter, and a 20- to 30-cm length can be harvested without much difficulty.

Number of fascicles. The number and size of fascicles should correlate between the donor and host nerves. The IAN usually has 18 to 21 fascicles in the third molar area, decreasing to about 12 fascicles just proximal to the mental foramen area (4, 5). The LN in the third molar area usually has 15 to 18 fascicles (6), decreasing to 9 fascicles as it enters the tongue (8). The sural nerve usually has 11 to 12 fascicles (7), which is 54% of the number of fascicles in the IAN and 69% of the number in the LN. The great auricular nerve usually has 8 to 9 fascicles (3), which is significantly less than the number in the IAN (44%) and LN (52%). However, if a cable graft with 2 parallel nerve graft strands is used (Figure 2), the combined number of fascicles correlates more closely with those of the IAN (87%) and LN (104%). Sometimes, the great auricular nerve is even smaller, and the transverse cervical nerve may be considered. If the nerve graft is significantly smaller in diameter than the proximal host nerve stump, fascicles are lost and a neuroma may form. If the graft is too large at the distal host nerve stump, then some of the regenerating nerve fascicles in the graft will be lost. If the distal portion of the graft is smaller than the distal portion of the host nerve, then a number of the fascicles in the distal portion of the host nerve will not regenerate.

Fascicular pattern. The IAN and LN have polyfascicular patterns; the fascicles have various sizes from small to large diameter, but without fascicular grouping (4–6). The sural nerve has an oligofascicular (uniform size) pattern, but with small-diameter fascicles (7). The great auricular nerve is a polyfascicular nerve
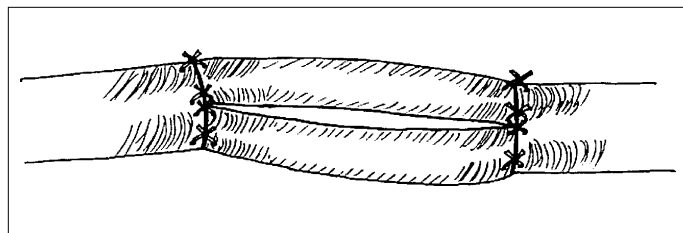
Figure 2. The cable grafting technique may be indicated to improve the match of graft to host nerve in cross-sectional diameter, number of fascicles, and fascicular pattern.

with grouping, a pattern that more closely approximates the fascicular pattern of the IAN and LN than the sural nerve (4). The axons in the sural nerve are much smaller and fewer in number than those in the IAN and LN, creating another significant mismatch.

Cross-sectional shape and area. The IAN and LN are round (4, 6), whereas the sural nerve is basically flat (6). The great auricular nerve is round-oval (4, 5). Therefore, the great auricular nerve more closely resembles the IAN and LN than does the sural nerve. The approximate total cross-sectional area of the IAN is 4.6 mm^2 (4, 5); the LN, 5.2 mm^2 (6); the sural nerve, 3.5 mm^2; and the great auricular nerve, 1.8 mm^2. There is no significant difference in fascicular and total nerve areas among the IAN, LN, and great auricular nerve (4, 5). The sural nerve has significantly smaller axonal size and number of axons per unit area (50% less) than the others (9).

Patient preference. Harvesting the sural nerve results in numbness of the heel and lateral aspect of the foot. Harvesting the great auricular nerve results in numbness to the ear, lateral neck, and skin overlying the posterior aspect of the mandible. An additional risk at the donor area is development of a painful neuroma that may require additional treatment. Patients may prefer that their numbness and/or potential complications be in the foot or in the head and neck area.

FACTORS AFFECTING NERVE GRAFT SUCCESS

The success and ultimate outcome of a nerve repair or grafting procedure are based on a number of factors. The more favorable the factors, the better and more predictable the outcome.

Time since the injury. Peripheral nerve injuries requiring surgical intervention will have better results the earlier the nerve is repaired after injury. Therefore, repairs with or without grafting done immediately after the injury have better results, with progressively worsening results if done 3, 6, 9, or 12 months or longer after the injury. Wietholter et al reported best results for IAN and LN repair if reconstruction was done within 3 weeks of the injury (10). Early repair circumvents major problems encountered with elapsed time such as Wallerian degeneration, atrophy, and fibrosis in the distal portion of the nerve. Atrophy creates a significant size match discrepancy between the nerve graft and either or both stumps. The time factor reflects the rate and extent of degeneration and atrophy of the distal fascicles prior to nerve repair. However, if the injury is primarily a traumatic neuroma without atrophy or degenerative neurologic changes in the distal portion of the nerve, the time factor may not be as important; that is, whether the repair is done at 3 weeks or 2 years may not make a difference in functional outcome.

Type and extent of injury. The more localized and confined the injury, the less trauma to the nerve, and the shorter the required nerve graft (or possibility of repair without grafting), then the better the outcome. Stretch injuries or injuries caused by injection of alcohol, steroid, or other caustic chemical into or adjacent to a nerve can cause significant irreversible damage to the nerve, which can extend proximally into the ganglion and cell bodies, beyond a surgically accessible area, thus rendering peripheral nerve repair ineffective.

Vascularity in the area. For a nerve graft to be successful, it must be revascularized quickly. Therefore, having the graft and the areas of anastomosis exposed to adjacent healthy soft tissues will help in this regard. Placing the graft inside a bony canal or in an area of significant scar tissue will predictably have poorer results because of delayed revascularization of the graft.

Orientation of nerve graft placement. It is important to place a nerve graft so that it is oriented in the same functional direction from which it was harvested. That is, the proximal end of the nerve graft should approximate the proximal end of the host nerve, and the distal end of the graft should anastomose with the distal end of the host nerve. Axonoplasmic flow should be maintained in the same direction. Therefore, when a nerve graft is harvested, the orientation should be carefully noted.

Length of nerve graft required. The shorter the nerve graft required, the better the result. The longer the nerve graft, the less predictable the result. This is due in part to the amount of time it takes for regeneration to occur across each anastomosis area (7–14 days) and along the length of the nerve (0.2–3 mm per day). The longer the nerve graft, the more time is required for regeneration to reach the distal anastomosis of the graft, increasing the risk of atrophy and fibrous ingrowth into the distal anastomosis area, resulting in a poorer outcome.

Quality and type of repair. Quality of repair is particularly sensitive to the surgeon's skill and experience. Obviously, the highest quality repairs yield the best results. A high-quality repair includes atraumatic management of the proximal and distal ends of the host and graft nerves. The TN branches are polyfascicular without grouping and have a large number of fascicles, so epineurial repair is the most logical and appropriate choice of technique. Depending on the situation, 8-0 to 11-0 monofilament nylon suture can be used for the repairs. Minimizing the number of sutures (3 to 6 is optimal) is helpful as long as the approximation of the graft to nerve stumps is accurate. It is important to try to suture only the epineurium and not pass the needle and suture through the fascicles, as this can create more damage and scarring, yielding a poorer result.

Tension on repaired nerve. The nerve should be repaired or grafted with no tension on the nerve segments and areas of anastomosis. Excessive tension can cause breakdown at the area of anastomosis, resulting in a poor outcome. The host nerve should be prepared prior to harvesting the graft so that graft length can be determined as accurately as possible. The cut host nerve will retract, yielding a larger defect. A harvested nerve graft shrinks in length by approximately 20%, and additional length may be lost in final preparation of host and nerve graft ends. Therefore, the nerve graft harvested should be 25% longer than the host nerve defect to compensate for these changes.

Preparation of the host nerve. A good result requires removal of the area of injury and assurance of healthy, viable nerve at the proximal and distal stumps. Frozen sections for histological assessment of the proximal and distal stumps may be helpful to determine when good, viable nerve tissue has been reached (11). In the distal end, there may be degenerative changes (Wallerian degeneration) involving the fascicles. However, it is important to be sure that no significant fibrosis or other obstructions remain in the distal portion of the host nerve.

Age of patient and other health factors. In general, young children have the best results and elderly patients the poorest results for nerve repair or grafting. Children have a greater ability to centrally adapt to altered nerve programming, greater regenerative capabilities, and greater healing and metabolic rates than older patients. Systemic factors that can adversely affect outcome include connective tissue and autoimmune diseases (e.g., scleroderma, mixed connective tissue disease, rheumatoid diseases, systemic lupus erythematosus), diabetes, vascular and bleeding disorders, inherited or acquired neuropathies, alcoholism, smoking, and others. These factors must be considered when counseling patients about risks, complications, and expected outcomes.

EXPECTED OUTCOMES

Many factors influence the quality of results. If the donor nerve and other success factors are all favorable, then good results can be expected. Definition of a successful and acceptable outcome varies widely among patients and surgeons. The quality of outcome for a given patient may not be predictable, but the more favorable the factors affecting success, the greater the potential for a good outcome. It must be understood that the best result may not restore function to the preinjury level. With LN injury, return of taste sensation should not be expected.

Wietholter et al found better results for IAN repair with end-to-end anastomosis than with nerve grafting (10). This has been the senior author's experience also. Therefore, with IAN injuries, the possibility of decortication of the mandible over the distal portion of the IAN should be evaluated, and the distal portion of the IAN and mental nerve should be posteriorly repositioned to facilitate end-to-end repair before considering a nerve graft. Hessling et al reported that only 40% of patients who underwent IAN reconstruction and 35% who underwent LN reconstruction had good results (12). They recommended reconstruction of these nerves only if the patient has pain in addition to loss of sensitivity. Zuniga reported on outcomes of nerve repair in 10 patients; both patients and surgeon rated the overall outcomes as mostly good, although there were differences in specific outcome ratings by surgeon and patients (13). Donoff and Colin reported improvement in 63% of their patients who underwent LN repair (31 nerves): 77% in the anesthesia group and 42% in the pain-paresthesia group (14). Improvement was seen in 77% of patients who underwent IAN repair.

Less favorable results in some studies may have been related to unfavorable factors affecting outcome. Assessment of the literature indicates that LN repairs are less successful than other nerve repairs. Perhaps difficulty in surgical access and constant mobility of the area after surgery (i.e., eating, swallowing, speaking) may contribute to the lower success rate. Also, the LN is the largest branch of the trigeminal system. Most surgeons use

only a single-strand graft for repair of any of the TN branches, resulting in a significant mismatch in size and fascicular characteristics, which may contribute to a less satisfactory outcome. Use of cable grafting may improve the results for some patients (1).

NERVE GRAFTING WITH OTHER TISSUES

Alternative tissues such as veins, collagen conduits and filaments, and perineurium tubes have been used for nerve repair. The majority of human studies have involved vein grafts. There are no studies on using vein grafts for repair of the TN branches. Tang, Gu, and Song reported on a technique in which a vein was taken from the forearm and reversed to bridge digital nerve defects (15). For nerve defects >2.0 cm, normal nerve slices were inserted inside vein conduits. Follow-up revealed excellent recovery in 2 digital nerves, good in 9, fair in 5, and poor in 2.

Chiu and Strauch reported a prospective comparative clinical study evaluating direct nerve repair, nerve grafting, and vein grafting for distal sensory nerve defects ≤3 cm (16). A total of 34 nerves were repaired: 15 with a venous nerve conduit, 4 with a sural nerve graft, and 15 with direct repair. Significant symptom relief and satisfactory sensory function return were observed in all patients. Two-point discrimination measurements indicated the superiority of direct repair, followed by conventional nerve grafting and then vein grafting. However, the universally favorable patient acceptance and the return of measurable 2-point discrimination indicated the effectiveness of autogenous vein grafts as nerve conduits when selectively applied to bridge a small nerve gap (≤3 cm) on nonessential peripheral sensory nerves.

Walton et al reported a retrospective study on the use of autogenous vein grafts in 22 digital nerve repairs (17). Two-point discrimination averaged 4.6 mm for 11 acute digital nerve repairs using vein conduits 1 to 3 cm in length. Delayed digital nerve repair with vein conduits yielded poor results. Comparing end-to-end digital nerve repairs and digital nerve grafting suggests that repair of 1- to 3-cm gaps in digital nerves with segments of autologous vein grafts appears to give results comparable to those of nerve grafting.

However, autogenous vein grafts have little mechanical resistance to kinking and collapse (11, 15). Tang, Shi, and Zhou demonstrated that repair of digital nerves with gaps ranging from 4 to 5.8 cm using vein conduits yielded no detectable recovery of sensibility in autonomous areas of these nerves and no sign of recovery of the innervated muscles during follow-up (18). Reexploration revealed that the vein conduits used for repair of the median nerves were constricted by surrounding scar tissue; axon regeneration was precluded.

ALLOPLASTIC NERVE GRAFTS
Permanent conduit materials

Silicone is a permanent conduit material that has been used for nerve grafting. However, long-term tubulization of a nerve produces localized compression with resultant decreased axonal conduction, although total number of nerve fibers and axon size remain constant. Alterations in the blood-nerve barrier occur, followed by demyelination of the nerve fibers (19, 20). Silicone tubes used for neural conduits must be removed to achieve a positive outcome (21). Similar unfavorable outcomes have been seen when using Gore-Tex vein grafts (WL Gore and Associates,
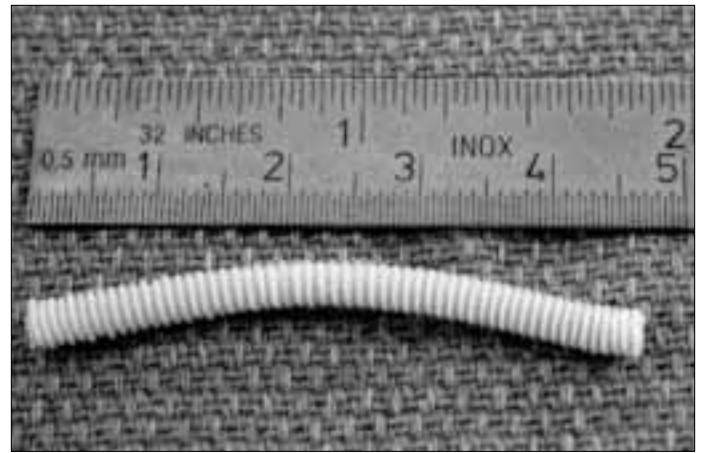
Figure 3. Neurotube is a corrugated conduit composed of polyglycolic acid with an internal diameter of 2.0 mm and a length of 4 cm.

Inc, Flagstaff, Ariz) as a nerve graft conduit (22, 23). The clinical studies indicated that Gore-Tex (polytetrafluorethylene) tubing is not effective and therefore not recommended in the repair of continuity defects of IAN and LN.

Synthetic resorbable conduits

Polyglycolic acid (Dexon, American Cyanamid Co, Wayne, NJ) is a bioabsorbable substance that is currently used as a suture material (24) and in mesh form to wrap internal organs injured as a result of trauma (25). It is absorbed in the body by means of hydrolysis within 90 days of implantation (26, 27).

A bioabsorbable polyglycolic acid conduit has been developed for nerve grafting (Neurotube, Neurogen LLC, Bel Air, Md) and was approved by the Food and Drug Administration for human use in 1999 (*Figure 3*). Characteristics of this tube include 1) porosity, which provides an oxygen-rich environment for the regenerating nerve; 2) flexibility, to accommodate movement of joints and associated tendon gliding; 3) corrugation, to resist the occlusive force of surrounding soft tissue; and 4) bioabsorbability, eliminating the need for removal at a subsequent operation. This corrugated tube has an internal diameter of 2.0 mm and a length of 4 cm.

Weber et al reported a prospective study on 136 nerve repairs in the hand, divided into 2 groups: group 1 consisted of standard repair with either end-to-end anastomosis or nerve graft, and group 2 consisted of nerve repair using a polyglycolic acid conduit (28). There were no statistical differences between the 2 groups overall. However, 2-point discrimination was better in the polyglycolic acid conduit group (6.8 ± 3.8 mm) than in the direct anastomosis or nerve graft group (12.9 ± 2.4 mm). The polyglycolic acid conduit provided superior results and eliminated donor-site morbidity.

Few articles have been published about Neurotube as an alloplastic material for TN repair. Crawley and Dellon reported an isolated case in which a 2.0-mm diameter polyglycolic acid bioabsorbable nerve conduit was used. A 51-year-old woman developed immediate and persistent numbness of the right lower lip and chin with no associated dysesthesia after extraction of a right mandibular molar tooth. Surgical repair of the right IAN was undertaken 16 months following the original extraction. The tube was filled with autologous serum to prevent blood clot for-

mation. After surgery, the patient suffered no further facial pain. Progressive improvement in sensation of the lower lip and chin was noted, beginning 6 months after surgery. At 12 months after surgery, pressure and vibratory perception were similar to those of the contralateral lip and chin area (29).

Since the polyglycolic acid conduit is resorbed, the problems associated with permanent tubing (i.e., Silastic, Gore-Tex), including compression and demyelination, are eliminated. The superior results achieved with this nerve grafting conduit are related to the elimination of the problems associated with a harvested nerve graft, host-donor differences in diameter, mismatches in number and pattern of fascicles and cross-sectional shape and area, and morbidity of the donor area. However, polyglycolic acid conduit grafting results will still be affected by such factors as time since injury, type and extent of injury, vascularity, graft size match, length of nerve graft required (results are good for defects ≤3 cm), quality of repair, tension on the repaired nerve, preparation of the host nerve, age of patient, and other health factors.

We have utilized the Neurotube conduit for IAN and LN grafting with good preliminary results. The technique we use includes preparation of the proximal and distal ends of the host nerve and of a conduit graft that is at least 1 cm longer than the size of the defect. Four 8-0 to 10-0 nylon sutures are passed through the tube 5 mm from the end, through the epineurium, and back out through the tube in a mattress fashion. After all sutures are passed, the sutures are then gently pulled to deliver the proximal end of the nerve within the tube. The same procedure is carried out for the distal end of the nerve. If there is a discrepancy in the sizes of host nerve end and tube diameter, the tube can be slit at the end to allow expansion or contraction to correlate to host nerve diameter. The artificial nerve conduit is then filled with a solution containing 1000 U of heparin per 100 mL of isotonic saline to help prevent blood clot formation, which could impede axonal regeneration.

SUMMARY

Nerve repairs and grafting techniques have been around for many years. Autogenous nerve grafts have worked reasonably well in the right circumstances but are associated with difficulties in achieving a proper donor-host match and with postsurgical sequelae at the donor site. Vein grafts appear to work almost as well as autogenous nerve grafts in digital nerve repairs that require a graft <3 cm in length. Currently, the most promising nerve graft material is the polyglycolic acid tube, which has shown better results than nerve grafting in early studies. Our initial experience supports this. However, more research studies using this material with other nerve repairs is essential to validate its superiority in these procedures.

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